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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,065	09/24/2003	David M. Markovitz	UM-08388	5111

72960 7590 02/04/2009

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
02/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,065	MARKOVITZ ET AL.	
	Examiner	Art Unit	
	LISA V. COOK	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,20,21 and 24-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,20,21 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants response to the Office Action mailed 4/11/08 is acknowledged (Paper filed 10/13/08). In the amendment filed therein claim 13 was modified. New claim 28 was added.

Claims 1-12, 15-19 and 22-23 have been canceled without prejudice or disclaimer.

Currently claims 13-14, 20-21, and 24-28 are pending and under consideration.

2. Rejections and/or objections of record not restated herein have been withdrawn.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 13-14, 20-21, and 24-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing mortality in mice via the administration of anti-vimentin antibodies 15 min prior to an *E. coli* (J-96) intraperitoneal injection (see examples 6 and 7 on pages 78-79), it does not reasonably provide enablement for any and all methods for reducing mortality in any and all subjects having any pathogen/sepsis via the administration of any and all anti vimentin antibodies.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets enablement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988).

Wands states on page 1404, "Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims."

Specifically the claims are drawn to a method of administering an anti-vimentin antibody to any and all subjects to treat any bacterial pathogen causing any and all sepsis. The specification teaches that anti-vimentin IgG antibodies may have a phagocytic and killing activity on MDM cells cultured *in vitro*. See page 72 lines 13-24 and example 4 on page 77, for example. The specification also exemplifies reduced *E.coli* septicemia and mortality. However, this reduction appears to *only* be seen if mice are administered anti-vimentin antibodies - 15 minutes prior to an *E. coli* (J-96) intraperitoneal injection (see examples 6 and 7 on pages 78-79).

These teachings do not enable one skilled in the art to effectively practice any and all methods for reducing mortality in any subject as set forth in the instant claims. For example, the method has not been demonstrated in humans.

The prior art teaches that the presence of anti vimentin antibodies is linked to detrimental results in patients. For example, the reference to Yang et al. (Clinical and Experimental Immunology, April 2002, Vol.128, No.1, pp 169-174) were high levels of antivimentin antibodies are linked to IPF (idiopathic pulmonary fibrosis), NSIP (non-specific interstitial pneumonia), systemic lupus erythematosus, progressive systemic sclerosis and RA. Thus from the prior art teaching the administration of anti-vimentin antibodies to a subject would appear to induce diseases and/or disorders since elevated levels are linked to adverse effects. This is contrary to the instant invention which is directed to reduced risk of mortality. See abstract and page 128 – Discussion.

Further, the specification does not set forth any *in vivo* data showing the protective ability of anti-vimentin antibody administration to a subject other than vimentin in mice with goat anti-vimentin serum. Example 7 on page 79 teaches that "mice receiving goat anti-vimentin show a 38% reduction in mortality compared to those receiving *anti-vimentin antibody* free serum (figure 9)". In addition, this is only exemplified in 13 week old mice with lethal dosages of *E. coli* (J-96) wherein the mice were injected with goat anti-vimentin serum 15 min prior to *E. coli* (J-96) injection. These particulars are not recited in the instant claims. Therefore the broad claim of killing any and all bacterial pathogens, in any and all subjects, with any and all anti-vimentin antibodies is not enabled.

The prior art teaches that species specific antibodies against vimentin have different reactivity. See abstract to Bohn et al. (Experimental Cell Research, Vol.201, No.1, July 1992, pages 1-7). The art also teaches that in vitro results can not predict in vivo antibody responses. See Pallini et al. (Journal of Neuro-Oncology, Vol. 49, 2000, pages 9-17). As such the reduction of mortality in any and all subjects having any pathogen/sepsis via the administration of any and all anti-vimentin antibodies is not apparent and would require undue experimentation.

Devoid of results supporting in vivo killing of any other pathogen/sepsis by other species of anti-vimentin antibodies, the skilled artisan would not be able to predict the outcome of the administration of the claimed anti-vimentin antibodies activity, i.e. would not be able to accurately predict if anti-vimentin antibodies agents would be useful in the claimed purpose.

The anti-vimentin antibody art is highly unpredictable and the instant specification fails to provide any information that anti-vimentin antibodies would protection (reduce mortality) in a human with a pathogen.

There are no immunological experiments provided to demonstrate that the claimed proteins or fragments are capable of mounting an efficient immune response and, more importantly, there are no challenge experiments to demonstrate that a person injected with any one of the claimed anti-vimentin antibodies would exemplify reduced mortality.

There are no protocols provided which demonstrate which anti-*vimentin antibodies* would be effective in reducing mortality in any and all pathogens, nor are there any protocols detailing the amount of antivimentin antibody needed to mount a sufficient reduction in mortality in any species other than mice.

There is no teaching as to what would be the other effective routes of administration for the claimed administered antibody (other than IP in mice). There is merely a general outline of agents/drug/antibody/vaccine and their administration, which does not directly apply to the instant invention. It is unclear that one of skill in the art could follow these general guidelines and achieve immunization (protection/treatment) of a human against all pathogens/sepsis without undue experimentation.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The ability to reasonably predict the capacity of a single bacterial immunogen to induce protective immunity from *in vitro* antibody reactivity studies is problematic.

Unfortunately, the art is replete with instances where even well characterized antigens that induce an *in vitro* neutralizing antibody response fail to elicit *in vivo* protective immunity. See Blasi et al. (Clinical Pulmonary Medicine, 2002, 9/1, 6-12 - Abstract) wherein *in vitro* data regarding *C. pneumonia* activity/treatment could not predict optimal dosing and length for in vivo activity/treatment.

Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful anti-*vimentin antibody* agent with out prior demonstration of efficacy in the particular diseases.

Specifically, anti-*vimentin antibodies* do not necessarily end up providing any protective immunoprotection and have actually been linked to various disease states. Yang et al. (Clinical and Experimental Immunology, April 2002, Vol.128, No.1, pp 169-174)

It has been set forth above that 1) the experimentation required to provide treatment of antivimentin antibodies to a mammal/human having *a pathogen* ad reducing the risk of mortality would be great as 2) there are no experiments provided to demonstrate that the claimed antibodies can be administered to achieve the claimed outcome in any subject other than mice and, more importantly, there are no challenge experiments to demonstrate that a person immunized with any one of the claimed anti-vimentin antibody agents would be protected from *a pathogen.*

There is insufficient evidence or nexus that would lead the skilled artisan to predict reducing mortality in any and all subjects having any pathogen/sepsis via the administration of any and all anti vimentin antibodies. In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which are reasonably predictive, commensurate in scope with the claimed invention, and in view of the teachings of In re Wands, 8 USPQ2d 1400; it has been determined that the level of experimentation required to enable the scope/breadth of the instant claims is undue.

Response to Arguments

Applicant amendments and arguments that the scope of enablement rejection directed to vaccine/immunization procedures was not on point. This argument was carefully considered and found persuasive. Accordingly the rejection has been modified to clearly address the enablement of only a method of reducing mortality in mice via the administration of anti-vimentin antibodies 15 min prior to an *E. coli* (J-96) intraperitoneal injection (see examples 6 and 7 on pages 78-79).

4. For reasons aforementioned, no claims are allowed.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300.

In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached on (571) 272-0806.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA or CANADA) or 571-272-1000.

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2/2/09

/Lisa V. Cook/
Primary Examiner, Art Unit 1641